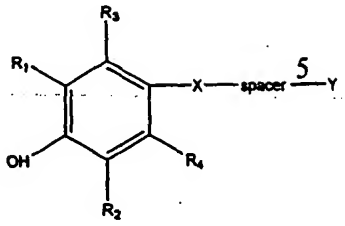
We claim:

1. A compound of formula (I)



(I)

wherein

X is O, S, SO, SO_2, CH_2, or NH;

Spacer is a group selected from the group consisting of $-(CH_2)_n-$, $-(CH_2)_n-CO-$, $-(CH_2)_n-N-$, $-(CH_2)_n-O-$, $-(CH_2)_n-S-$, $-(CH_2O)-$, $-(OCH_2)-$, $-(SCH_2)-$, $-(CH_2S-)$, -(aryl-O)-, -(O-aryl)-, -(alkyl-O)-, -(O-alkyl)-;

n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

Y is substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted alkylthio, substituted or unsubstituted alkylthioalkyl, substituted or unsubstituted alkylsulfinyl, substituted or unsubstituted alkylsulfinylalkyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted alkylsulfonylalkyl, NH_2, NHR, NR_2, SO_2-OH, OC(O)R, C(O)OH, C(O)OR, $C(O)NH_2$, C(O)NHR, $C(O)NR_2$, SO_2NH_2, SO_2NHR, SO_2NR_2;

R is alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, alkyl-COOH, alkyl-COOalkyl, alkyl-COOaryl, heteroaryl, substituted heteroaryl, or when attached to a nitrogen atom, two adjacent R groups may combine to form a ring of 5 to 7 members;

R^1 and R^2 are independently straight chained, branched, or cyclic alkyl which may be substituted, aryl, substituted aryl, heteroaryl, substituted heteroaryl, alkaryl, or aralkyl; and wherein substituents on the R^1 or R^2 groups are selected from the group consisting of hydrogen, halogen, alkyl, nitro, amino, alkylamino, dialkylamino, acyl, and acyloxy;

R^3 and R^4 are independently any group that does not otherwise adversely affect the desired properties of the molecule, or R^1; or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1, wherein X is S, SO, or SO_2; Spacer is $-(CH_2)_n-$ or $-(CH_2)_n-CO-$; n is 0-10; Y is aryl, substituted aryl, heteroaryl, substituted heteroaryl, NH_2, NHR, NR_2, alkyl, substituted alkyl, acyloxy, and substituted acyloxy; R is alkyl, alkenyl, alkynyl, aryl, alkyl-COOH, alkyl-COOalkyl, alkyl-COOaryl, heteroaryl, or nitro substituted heteroaryl, or when attached to a nitrogen atom, two adjacent R groups may combine to form a ring of 5 to 7 members; R^1 and R^2 are independently straight chained, branched or cyclic C_{1-5} alkyl; R^3 and R^4 are independently H, or a pharmaceutically acceptable salt thereof.

3. The compound of claim 2, or a pharmaceutically acceptable salt thereof, selected from the group consisting of compounds of formula (I) wherein

X=S; R^1=t-butyl; R^2=t-butyl; R^3=H; R^4=H; Spacer=$-CH_2-$; Y=4-carboxymethylphenyl;

X=S; R^1=t-butyl; R^2=t-butyl; R^3=H; R^4=H; Spacer=$-CH_2-$; Y=4-nitrophenyl;

X=S; R^1=t-butyl; R^2=t-butyl; R^3=H; R^4=H; Spacer=$-(CH_2)_2-$; Y=4-nitrophenyl;

X=S; R^1=t-butyl; R^2=t-butyl; R^3=H; R^4=H; Spacer=$-CH_2-$; Y= 2-carboxyethyl;

X=S; R^1=t-butyl; R^2=t-butyl; R^3=H; R^4=H; Spacer=$-CH_2-$; Y=3,5-di-t-butyl-4-carboxypropanoyloxy;

X=S; R^1=t-butyl; R^2=t-butyl; R^3=H; R^4=H; Spacer=$-CH_2-$; Y=4-carboxyphenyl;

X=S; R^1=t-butyl; R^2=t-butyl; R^3=H; R^4=H; Spacer=$-CH_2-$; Y=1-acetyloxy-1-methylethyl;

X=S; R^1=t-butyl; R^2=t-butyl; R^3=H; R^4=H; Spacer=$-CH_2-$; Y=3-nitrophenyl;

X=S; R^1=t-butyl; R^2=t-butyl; R^3=H; R^4=H; Spacer=$-CH_2-$; Y=2,4-dinitrophenyl;

X=S; R^1=t-butyl; R^2=t-butyl; R^3=H; R^4=H; Spacer=$-CH_2-$; Y=4-trifluoromethylphenyl;

X=S; R^1=t-butyl; R^2=t-butyl; R^3=H; R^4=H; Spacer=$-CH_2-$; Y=2-carboxyfuranyl;

X=S; R^1=t-butyl; R^2=t-butyl; R^3=H; R^4=H; Spacer=$-CH_2-$; Y=4-(N,N-dimethyl)sulfonamidophenyl;

X=SO; R^1=t-butyl; R^2=t-butyl; R^3=H; R^4=H; Spacer=$-CH_2-$; Y=4-nitrophenyl;

X=SO_2; R^1=t-butyl; R^2=t-butyl; R^3=H; R^4=H; Spacer=$-CH_2-$; Y=4-nitrophenyl;

X=S; R^1=t-butyl; R^2=t-butyl; R^3=H; R^4=H; Spacer=$-CH_2-$; Y=4-acetyloxyphenyl;

X=S; R^1=t-butyl; R^2=t-butyl; R^3=H; R^4=H; Spacer=$-CH_2-$; Y=4-methylphenyl;

X=S; R^1=t-butyl; R^2=t-butyl; R^3=H; R^4=H; Spacer=$-CH_2-$; Y=4-fluorophenyl;

X=S; R^1=t-butyl; R^2=t-butyl; R^3=H; R^4=H; Spacer=$-CH_2-$; Y=ethylsulfonic acid;

X=S; R^1=t-butyl; R^2=t-butyl; R^3=H; R^4=H; Spacer=$-CH_2-$; Y=2-dimethylaminomethyl;

X=S; R^1=t-butyl; R^2=t-butyl; R^3=H; R^4=H; Spacer=$-(CH_2)_3-$; Y=dimethylamino;

X=S; R^1=t-butyl; R^2=t-butyl; R^3=H; R^4=H; Spacer=$-(CH_2)_5-$; Y=acetyloxy; and

X=S; R^1=t-butyl; R^2=t-butyl; R^3=H; R^4=H; Spacer=$-CH_2-$; Y=4-(2-hydroxy)ethylphenyl.

4. A pharmaceutical composition for the treatment of a disease mediated by the expression of VCAM-1, comprising an effective amount of a compound of any one of claims 1, 2 or 3 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

5. A method for the treatment of a disorder mediated by the expression of VCAM-1, comprising administering to a patient an effective amount of a compound of formula (I) as claimed in any one of claims 1, 2 or 3, or a pharmaceutically acceptable salt thereof, optionally in a pharmaceutically acceptable carrier.

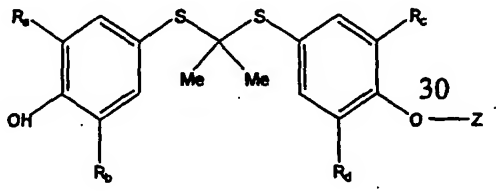
6. The method of claim 5, wherein the disorder is a cardiovascular disorder.

7. The method of claim 6, wherein the cardiovascular disorder is selected from the group consisting of atherosclerosis, post-angioplasty restenosis, coronary artery disease, angina, or small artery disease.

8. The method of claim 5, wherein the disorder is an inflammatory disease.

9. The method of claim 8, wherein the inflammatory disease is selected from the group consisting of rheumatoid arthritis, osteoarthritis, asthma, dermatitis, multiple sclerosis and psoriasis.

10. A compound of formula (II)



(II)

wherein

R_a, R_b, R_c, and R_d are independently any group that does not otherwise adversely affect the desired properties of the molecule selected from the group consisting of hydrogen, straight chained, branched, or cyclic alkyl which may be substituted, aryl, substituted aryl, heteroaryl, substituted heteroaryl, alkaryl, substituted alkaryl, aralkyl or substituted aralkyl; substituents on the R_a, R_b, R_c and R_d groups are selected from the group consisting of hydrogen, halogen, alkyl, nitro, amino, haloalkyl, alkylamino, dialkylamino, acyl, and acyloxy;

Z is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, aralkyl, alkaryl, heteroaryl, heteroaralkyl, a carbohydrate group, $-(CH_2)-R_e$, $-C(O)-R_g$, and $-C(O)-(CH_2)_n-R_h$, wherein (a) when each of R_a, R_b, R_c, and R_d are t-butyl, Z cannot be hydrogen and (b) when each of R_a, R_b, R_c, and R_d are t-butyl, Z cannot be the residue of succinic acid;

R_e is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, alkoxy, substituted alkyloxy, alkoxyalkyl, substituted alkoxyalkyl, NH_2, NHR, NR_2, mono- or polyhydroxy-substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, acyloxy, substituted acyloxy, COOH, COOR, $-CH(OH)R_k$, hydroxy, $C(O)NH_2$, C(O)NHR, $C(O)NR_2$;

R_g is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, alkoxy, substituted alkyloxy, alkoxyalkyl, substituted alkoxyalkyl, NH_2, NHR, NR_2, mono- or polyhydroxy-substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

R_h is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, alkoxy, substituted alkyloxy, alkoxyalkyl, substituted alkoxyalkyl, NH_2, NHR, NR_2, mono- or polyhydroxy-substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, acyloxy, substituted acyloxy, COOH, COOR, $-CH(OH)R_k$, hydroxy, O-phosphate, $C(O)NH_2$, C(O)NHR, $C(O)NR_2$ and pharmaceutically acceptable salts thereof;

Or, in an alternative embodiment, R_e, R_g, and R_h can independently be a substituent which improves the water solubility of the compound, selected from the group consisting

of C(O)-spacer-SO_3H, wherein spacer is as defined above, C(O)-spacer-SO_3M, wherein M is a metal used to form a pharmaceutically acceptable salt, C(O)-spacer-PO_3H_2, C(O)-spacer-PO_3M_2, C(O)-spacer-PO_3HM, C(O)-spacer-PO_4H, C(O)-spacer-PO_4M, SO_3M, -PO_3H_2, -PO_3M_2, -PO_3HM, cyclic phosphates, polyhydroxyalkyl, carbohydrate groups, C(O)-spacer-$[O(C_{1-3}\ alkyl)_p]_n$, wherein n is as defined above and p is 1, 2, or 3, -$[O(C_{1-3}\ alkyl)_p]_n$, carboxy lower alkyl, lower alkylcarbonyl lower alkyl, N,N-dialkyl amino lower alkyl, pyridyl lower alkyl, imidazolyl lower alkyl, morpholinyl lower alkyl, pyrrolidinyl lower alkyl, thiazolinyl lower alkyl, piperidinyl lower alkyl, morpholinyl lower hydroxyalkyl, N-pyrryl, piperazinyl lower alkyl, N-alkyl piperazinyl lower alkyl, triazolyl lower alkyl, tetrazolyl lower alkyl, tetrazolylamino lower alkyl, or thiazolyl lower alkyl or a pharmaceutically acceptable salt thereof.

11. The compound of claim 10, wherein R_a, R_b, R_c, and R_d are independently hydrogen or straight chained, branched, or cyclic C_{1-10} alkyl; Z is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, a carbohydrate group, -(CH_2)-R_e, -C(O)-R_g, and -C(O)-$(CH_2)_n$-R_h, and a pharmaceutically acceptable salt thereof, provided that (a) when each of R_a, R_b, R_c, and R_d are t-butyl, Z cannot be hydrogen and (b) when each of R_a, R_b, R_c, and R_d are t-butyl, Z cannot be the residue of succinic acid.

12. The compound of claim 11, or a pharmaceutically acceptable salt thereof, selected from the group consisting of compounds of formula (II) wherein

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=4-nitrophenyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=CO-$(CH_2)_2$-COOH;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=CO-(5-nitrofuran-2-yl);

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=3-carboxypropyl;

R_a=1-methylethyl, R_b=t-butyl, R_c=methyl, and R_d=methyl; Z=4-aminobutyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=4-aminobutyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=3-hydroxypropanoyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=t-butylcarbonyloxymethyl;

R_a=t-butyl, R_b=t-butyl, R_c=H, and R_d=H; Z=4-aminobutyl;

R_a=t-butyl, R_b=t-butyl, R_c=H, and R_d=H; Z=3-carboxypropyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=carboxymethyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=2-($CONH_2$)ethanoyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=CO-aminomethyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=CO-(2-carboxyethyl);

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=CO-(2-methoxycarbonylethyl);

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=CO-aminomethyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=CO-3-carboxypropyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=3-carboxypropyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=CO-2-carboxyethyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=CO-ammonium methyl (chloride)

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=2-hydroxy-2-oxiranyl-ethyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=3-hydroxymethyloxirany-2-ylmethyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=3-(2-hydroxy-2-oxiranyl)ethoxyoxiran-2-ylmethyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=oxiranylmethyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=2-hydroxy-3-carboxymethylaminopropyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=2,3,4-trihydroxybutyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=2-hydroxy-3-ethoxypropyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=2,3-dihydroxypropyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=ethyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=2-ethoxycarbonylethenyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=4-N,N-dimethylaminophenethyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=CO-2-carboxyethyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=CO-2-carboxyethyl (L-arginine ester);

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=3-methoxycarbonylpropyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=2-carboxyethenyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=galactopyranosylmethyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=3-(N-N-diethylamino)propyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=2-ethoxycarbonylethenyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=carboxymethylaminocarbonylmethyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=1,3-dicarboxypropylaminocarbonylmethyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=2-hydroxy-3-(1,3-diethoxycarbonyl)propylaminopropyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=2,3-dihydroxy-4-carboxymethylaminobutyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=2-hydroxy-3-(5-amino-5-carboxy)propylaminopropyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=4-ethylcarbonyloxybutyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=4-hydroxybutyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=glucopyranosylmethyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=CO-3-tetrazolylpropyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=3-hydroxypropenyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=CH_2CONH-$(CH_2)CH(NH_2)COOH$;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=$CH_2CONHCH(COOet)CH_2CH_2(COOet)$;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=glucopyranosylmethyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=2,3,4,5,6-pentahydroxyhexane;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=CO-3-(2-hydroxyphenyloxyphosphoxy)propyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=CO-2,2-dimethyl-3-hydroxypropyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=2-hydroxy-3-acetoxypropyl;

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=2-acetoxy-3-hydroxypropyl; and

R_a=t-butyl, R_b=t-butyl, R_c=t-butyl, and R_d=t-butyl; Z=$CH_2CH(OH)CH_2NH$(2,3,4,5,6-pentahydroxyhexane.

13. A pharmaceutical composition for the treatment of a disorder mediated by the expression of VCAM-1 comprising an effective amount of a compound of any one of claims 10, 11 or 12, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

14. A method for the treatment of a disorder mediated by the expression of VCAM-1 comprising administering to a patient an effective amount of a compound of any one of

claims 10, 11 or 12, or a pharmaceutically acceptable salt thereof, optionally in a pharmaceutically acceptable carrier.

15. The method of claim 14, wherein the disorder is a cardiovascular disorder.

16. The method of claim 15, wherein the cardiovascular disorder is selected from the group consisting of atherosclerosis, post-angioplasty restenosis, coronary artery disease, angina, and small artery disease.

17. The method of claim 14, wherein the disorder is an inflammatory disease.

18. The method of claim 17, wherein the inflammatory disease is selected from the group consisting of rheumatoid arthritis, osteoarthritis, asthma, dermatitis, multiple sclerosis and psoriasis.

19. The method of claim 6, comprising administering the compound in combination with another cardiovascular drug selected from the group consisting of lipid lowering agents, platelet aggregation inhibitors, antithrombotic agents, calcium channel blockers, angiotensin converting enzyme (ACE) inhibitors, and β-blockers.

20. The method of claim 15, comprising administering the compound in combination with another cardiovascular drug selected from the group consisting of lipid lowering agents, platelet aggregation inhibitors, antithrombotic agents, calcium channel blockers, angiotensin converting enzyme (ACE) inhibitors, and β-blockers.

21. The method of claim 8, comprising administering the compound in combination with another antiinflammatory drug.

22. The method of claim 16, comprising administering the compound in combination with another antiinflammatory drug.